

Abstracts

Oral 3

Epidemiological methods and data analysis

03.1 ATTRIBUTABLE FRACTIONS IN MULTI-EXPOSED: QUANTIFYING CONTRIBUTIONS OF INDIVIDUAL RISK FACTORS

G. E. Eide¹, I. Heuch². ¹Centre for Clinical Research, Haukeland University Hospital & Section for Epidemiology and Medical Statistics, Department of Public Health and Primary Health Care, University of Bergen; ²Department of Mathematics, University of Bergen, Bergen, Norway

Introduction: Various methods have been proposed in the literature for quantifying the contributions of individual risk factors to a combined attributable fraction in a population, leading to concepts like the sequential attributable fractions, the average attributable fractions, the extra attributable fractions, and the rate fractions. It may be unclear how these concepts are to be interpreted and whether they apply also to attributable fractions in multi-exposed subpopulations.

Methods: These issues are clarified by using probabilistic reasoning and application of the various methods to synthetic examples as well as two published data sets from occupational medicine.

Results: Both theoretically and in practice the sequential and average attributable fractions have favourable properties compared with the extra attributable fractions and the rate fractions. Among these properties is additivity and completeness of partitioning. Also, a relation between the average attributable fractions in a population and in exposed is established.

Conclusion: Average attributable fractions represent a coherent methodology for apportioning attributable fractions in individuals, groups of individuals, and populations.

03.2 META-ANALYSIS IN OCCUPATIONAL EPIDEMIOLOGY FOR RARE DISEASE OUTCOMES: WHAT TO DO WHEN THERE ARE NO EXPOSED CASES?

D. M. McElvenny¹, B. G. Armstrong. ¹Public and Environmental Health Research Unit, London School of Hygiene & Tropical Medicine, UK

Introduction: Meta-analyses involving rare diseases, frequently involve cohort studies that report only a few observed cases with a correspondingly small expected number of cases. Problems occur when some studies report no observed cases ($\log(RR)$ is undefined), in particular if they do not provide an expected number of cases, or do not report a result for the disease of interest. The aim of this presentation is to examine the possible influence that such occurrences might have on inferences drawn from meta-analyses of rare disease outcomes.

Methods: We simulated Poisson data from 30 cohort studies, each with $E=1$ and $RR=1$. This resulted in 13 of the studies having zero observed cases, nine having one case, four having two cases, three having three cases, and one having four cases. We applied the usual meta-analysis methods of analysis, to assess the possible impact on inferences, of exclusion of the results with zeros, and their inclusion by adding constants 0.5, 0.1, 0.01, and 0.001 to all the observed and expected cases.

Results: The "true" meta-RR based on an analysis on the original scale via simply summing the observed and expected cases was 1.00 (95% CI 0.67 to 1.43). The meta-RR, based on analyses on the log scale, for the analysis excluding the zeros was 2.01 (1.41 to 2.88). The results, again via analyses on the log scale, where the zeros were incorporated by the addition of the small constants were respectively 1.30 (0.97 to 1.74), 1.69 (1.20 to 2.38), 1.96 (1.37 to 2.79), and 2.00 (1.40 to 2.89).

Conclusions: Excluding studies with zero exposed cases leads to upward bias, possibly considerable, on the summary RR when no association exists. Somewhat counter intuitively, results from analyses which added the smallest constant to the observed and expected cases produced results furthest from the "truth". Standard meta-analytical methods for rare disease outcomes, when there are a number of studies with zero

observed cases, and for which analyses are carried out on the log scale, should therefore be used with extreme caution.

03.3 EXPOSURE TO A TWO COMPONENT DUST: LONGITUDINAL ANALYSIS OF FVC USING GEE MODELS IN A COALWORKER INCEPTION COHORT FOLLOWED 1974-98

S. F. Büchte¹, P. Morfeld¹, J. Ambrosy³, H. Bicker³, H. Lenaerts³, B. Kalkowsky³, J. Pohlplatz³, A. Kösters^{1,2}, M. Rütter^{1,2}, C. Piekarski¹. ¹Institute for Occupational Sciences of RAG AG, Germany; ²Occupational Health Service, DSK AG, Herne, Germany

Introduction: Coalmine dust is recognised as a multicomponent dust containing a quartz and a non-quartz fraction. This study aims at a discriminating longitudinal analysis of lung function after exposure to these two dust components.

Methods: An inception cohort of German coalminers was enumerated. Exposure to each of the two components of respirable coalmine dust (RCMD) was determined on the basis of underground stationary dust samples. Dust samplers sampled according to the Johannesburg Convention. Silica concentrations in the RCMD were obtained from infrared spectroscopy. Repeated lung function measurements were re-evaluated by physicians. Longitudinal analyses on the change in FVC using generalised estimation equation models (GEE) were performed including as covariates: cumulative RCMD exposure (separated into a quartz and a non-quartz component), smoking information, height, age, mine, nationality, calendar time, and type of lung function measurement. Different correlation structures and different variable transformations were applied.

Results: The cohort comprised 1369 miners with 22 975 data entries on exposure history. The personal mean long term exposure intensity was 2.0 mg/m³ ($s=0.53$ mg/m³) (RCMD) and 0.07 mg/m³ ($s=0.03$ mg/m³) (respirable quartz dust). 7663 lung function measurements were available. The GEE (exchangeable working correlation matrix) returned an estimated FVC decrease of 0.06 l per 1000 mg*shift/m³ of non-quartz dust but an increase of 0.12 l per 100 mg*shift/m³ of quartz dust (both clearly significant). GEE results varied with correlation structures and variable transformations.

Conclusion: This study is the first to present results from a longitudinal analysis of change in lung function for an inception cohort from the hard coal mining industry. The GEE (exchangeable) revealed a negative association with the non-quartz component but—against expectation—a positive with the quartz component. However, model specification is crucial. Conclusions on the impact of correlated exposures should not be based on a single model, even if the findings are clearly significant.

03.4 BLADDER CANCER RISK IN SALES WORKERS: ARTIFACT OR CAUSE FOR CONCERN?

A't. Mannelje, N. Pearce. Centre for Public Health Research, Massey University, Wellington, New Zealand

Introduction: A surprisingly large number of epidemiological studies have reported positive associations between bladder cancer and sales occupations. This association has often been labelled a chance finding that lacks biological plausibility, and could be the result of confounding by smoking. Alternatively, it could be the result of low frequency of urination or exposure to carcinogens related to some sectors of sales work.

Methods: We reviewed the literature for studies reporting bladder cancer risk estimates for sales occupations. We used meta-analytical techniques to: (i) assess heterogeneity in the published associations between sales work and bladder cancer; (ii) assess reporting bias; (iii) identify a homogeneous group of risk estimates that could be considered independent of confounding or reporting bias; and (iv) derive a summary estimate.

Results: We identified 16 publications, reporting a total of 76 bladder cancer risk estimates for sales work, of which 20 were statistically significant. A meta-analysis including all published associations, showed elevated summary estimates for both men (OR 1.15, 95% CI 1.02 to 1.29) and women (OR 1.36, 95% CI 1.11 to 1.67). These estimates were highly heterogeneous (p_{Q-test} 0.00 and 0.03) and showed evidence of publication bias ($p_{Egger-test}$ 0.46 and 0.00). When the analysis was

restricted to incidence case control studies that adjusted for smoking and had reported their results irrespective of the strength of the association, the findings were no longer heterogeneous and did not show statistically significant publication bias. The summary estimate for men was 1.00 (95% CI 0.91 to 1.09), whereas the estimate for women was still (non-significantly) elevated (OR 1.18, 95% CI 0.99 to 1.39). For women, three studies also reported a positive duration response association for employment in sales and bladder cancer.

Conclusions: Reporting bias has caused an overrepresentation of statistically significant positive associations for sales work and bladder cancer in the literature. When reporting bias and confounding by smoking were taken into account, sales work did not entail an increased bladder cancer risk for males, but a small non-statistically significant increase in bladder cancer risk was observed for women.

03.5 RELIABILITY AND VALIDITY OF A GENERIC JOB EXPOSURE MATRIX APPLIED TO EPOXY RESIN EXPOSED MEXICAN WORKERS

L. Haro-García¹, G. Celis-Quintal², P. López-Rojas². ¹*Salud en el Trabajo, Universidad Nacional Autónoma de México, México;* ²*Instituto Mexicano del Seguro Social, México*

Introduction: The use of the job exposure matrix (JEM) is well justified in small enterprises where the measures to perform an environment and/or individual surveillance are limited and records do not exist. Despite these

evident advantages, it is necessary to evaluate the reliability of a these generic matrixes and to discuss validity.

Methods: We applied, concurrently and by two observers, the JEM created by the American Industrial Hygiene Association in 1988. The JEM includes evaluation in six sections and the structure of two axes: (1) exposure calculated for workplace, and (2) estimated calculation of health effects due to exposure of an occupational environmental agent. These axes allowed us to determine generically the exposure level to occupational environment agents from trivial to very high in 31 workers who employed epoxy resin during production at a small business in Mexico City. Observations of the JEM of both observers were subject to agreement percentage calculation (%C), kappa test (k_w), and intraclass correlation coefficient (ICC).

Results: %C and k_w were 64% and 0.58, respectively; disagreement was present in four of six matrix sections: "number of exposed individuals exposed", "level of exposure in relation to permissible exposure level (PEL)", "proximity to exposure source", and "means of control for occupational exposure". Nonetheless, the axes that determined exposure level, k_w were 0.62 and 0.54, respectively. The ICC demonstrated that the JEM section on "number of exposed individuals" and the axis denominated "estimated classification of health effects" showed the greatest interobserver variability.

Conclusions: Despite disagreement in some sections, final reliability of the JEM employed is at an acceptable level. These disagreements are susceptible to being diminished in that the JEM is sufficiently transparent to allow identification of sources of inconsistency, in addition to complying with the attributes of face validity and content validity.